

COMPOSITIONS AND METHODS TO INHIBIT
FORMATION OF THE C5b-9 COMPLEX OF COMPLEMENT

Abstract of the Invention

Compounds modulating CD59 mediated complement activity,

compositions including these compounds, and methods of making and using the compounds are disclosed, which are based on the identification of the hu CD59 amino acid residues which serve as the binding site for CD59-C9 interactions. These residues correspond to amino acid residues 42-58, and bind to the region of C9 corresponding to human 334-418, more specifically, between amino acid residues 359 and 384. Compounds can be derived using this basic amino acid sequence and corresponding three dimensional structure within the protein using any of several techniques known to those skilled in the art, including rational drug design using computer data bases and modeling of peptide/protein-ligand binding, antibodies and anti-idiotypic antibodies generated to the proteins or peptides containing this peptide sequence, and modified peptides. Those compounds imitating the structure and/or function of the peptide region are referred to herein as "peptidomimetics", and include small molecules which present the surface exposed side chains in these amino acids in the same relative positions, compounds identified by combinatorial chemistry techniques which bind to the active portions of human C9, as well as modified peptides. The compounds can be used to inhibit complement by binding to C9 analogously to CD59, or to maintain complement inhibition, by blocking CD59 binding to C9. The compounds can be administered locally or systemically in any suitable carrier in an amount effective to either inhibit complement or block the inhibition of complement, in a patient in need of treatment thereof.

866020-E6E02060